

### **REMARKS**

Applicant would like to thank the Examiner for discussing by telephone the application with the Applicant and Applicant's representatives on May 19, 2005. Part of the substance of the discussion is incorporated herein.

Claims 1-14 were previously pending and are still pending in this application. No new matter has been added.

### **Rejections Under 35 U.S.C. §102**

The Examiner maintained the rejection of claims 1-3, 6-10 and 13-14 under 35 U.S.C. §102(e) as anticipated by Mechanic U.S. patent 5,332,475 ("Mechanic '475") and reiterated the same arguments made in the Office Action dated August 17, 2004. According to the Examiner, "Mechanic (col. 2, lines 42-68; col. 3, lines 1-2 col. 4, lines 19-53) discloses using collagen fibrils or finely ground bovine skin collagen in a cross-linking process not subjected to an acid dissolution to make collagen fiber/fabric/matrix to be used inside a human being as an implant. Inherently, the product to be used inside a human body must have been sterilized."

The Examiner further stated that "Mechanic - '475 (col. 4, lines 38-64) clearly discloses a process comprising using collagen suspended in "buffer media (which has a pH in a range of 6.8 to 8.6) such as water (pH about 7)." (emphasis added). The Examiner further asserted that "Mechanic - '475 (col. 4, lines 50-64) clearly specif[ies] water as a suitable medium for suspension of a proteinaceous material without denaturation effect to the proteinaceous material." The Examiner asserted that there is no language or feature to distinguish the present invention over Mechanic.

Applicant had previously amended independent claim 1 to overcome the 35 U.S.C. §102 rejection of the claims as being anticipated by Mechanic '475. In particular, Applicant amended claim 1 by adding the limitation "wherein the collagen fibrils have been suspended in water" to distinguish over Mechanic '475. Based on the teachings of the Mechanic '475, its parent patent (U.S. patent 5,147,514 ("Mechanic '514")), and a review of the file history of both patents, Applicant previously argued that the above amendment would distinguish over Mechanic for the following reason.

The Mechanic '475 and '514 patents and their file histories suggest that it is important to place collagen in a buffered medium because a pH below neutral (about 7.0) jeopardizes the integrity of collagen fibrils. Thus, although the Mechanic '475 broadly discloses placing proteinaceous material in an aqueous medium that could be water, a suspension of collagen in water would not result in a suspension having a neutral to alkaline pH as set forth in Mechanic. When one places collagen fibrils in water, the result is a suspension which has an acidic pH. This is due to the acidic nature of the collagen molecules and the non-buffering capacity of water. Please note that the Applicant previously submitted (on September 4, 2001) a Declaration by Stephen Eldridge as evidence of the acidic pH that is obtained when collagen fibrils are suspended in water.

There are no further teachings in Mechanic '475 to suggest using water to suspend collagen. All of the examples in Mechanic '475 involve suspending collagen in aqueous buffered solutions. All of the Mechanic '475 claims require performing a cross-linking step in an aqueous buffer such that the pH is maintained between about 6.8 and about 8.6 or in a buffered medium having a neutral to alkaline pH.

In view of the above, Applicant argued that because water is not a buffer and because Mechanic '475 does not teach using non-buffered water or non-buffered aqueous media to suspend collagen, the above-recited amendment to independent claim 1 should overcome the §102 rejection. The Examiner is referred to the prior responses submitted by the Applicant on May 17, 2004 and February 17, 2005 for further elaboration on Applicant's above-presented arguments and reasoning.

Applicant's prior responses and the submitted supporting documentation were considered by the Examiner but were not found to be persuasive. The Examiner disagreed with the Applicant's statement that water is not a buffer medium. The Examiner argued that Mechanic discloses proteinaceous material being suspended in aqueous media such as water (having pH of from about 6.8 to 8.6) to avoid denaturalization of the collagen. According to the Examiner, (emphasis added) "water having a pH about 7 (neutral) which is well within the pH range of 6.8 – 8.6 disclosed by Mechanic –'475, must be considered as a buffer medium."

During the May 19, 2005 telephone discussion, the Examiner maintained his position that water can be a buffer, and thus, Mechanic anticipates the instant claims. Applicant's

representatives and Stephen Eldridge, an inventor, disagreed with the Examiner and reiterated that water alone is not a buffer and has no buffering capacity. Mr. Eldridge and Applicant's representatives further explained to the Examiner that the invention is directed to methods to form a collagen product (and the products produced thereby) which involve suspending collagen in water and avoiding acid dissolution. Although water itself is a pH neutral liquid, collagen fibrils are acidic and, when collagen is suspended in water, the pH of the resulting suspension is in the acidic range. The pH of a collagen suspension in water is acidic because water does not have a buffering capacity.

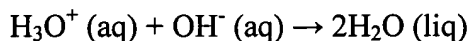
The Examiner maintained his position that water may be a buffer and suggested that the best way to overcome the rejections over Mechanic is for the Applicant to provide evidence that water is not a buffer. Applicant herewith submits the definitions of "buffers" copied from Remington's Pharmaceutical Sciences, 18<sup>th</sup> edition, 1990 (Exhibit 1) and from Chemistry for Engineers and Scientists, 1990 (Exhibit 2).

Remington's definition of "Buffers" states (beginning at line 45, page 241, emphasis added):

"If an acid or base is added to water, the pH of the latter is changed markedly, for **water has no ability to resist change of pH; it is completely devoid of buffer action.** Even a very weak acid such as carbon dioxide changes the pH of water, decreasing it from 7 to 5.7 when the small concentration of carbon dioxide present in air is equilibrated with pure water. This extreme susceptibility of distilled water to a change of pH on adding very small amounts of acid or base is often of great concern in pharmaceutical operations. Solutions of neutral salts, such as sodium chloride, similarly lack ability to resist change of pH on adding acid or base; such solutions are called unbuffered."

The definition of "Buffers" in Chemistry for Engineers and Scientists states (beginning at line 7, page 449, emphasis added):

**"When an acid or a base, even in relatively small amounts, is added to water, there is a large change in the pH of the solution.** For example, addition of as little as 0.010 mol of HCl lowers the pH of solvent water from 7 to 2, a change of 5 pH units. A buffer is a solution that is capable of absorbing excess acid or base without major changes in pH. Because such a solution must be able to react with a large fraction of added acid or base, **the buffer solution must contain both an acid and a base.** However, neither can be strong, since they would simply neutralize each other:



Instead, a buffer must contain a weak acid and a weak base. More specifically, a buffer must contain a weak acid and its conjugate base."

As is clear from the above two definitions of buffers, water is not a buffer and has no buffering capacity. Accordingly, the claims as currently pending are not anticipated by the Mechanic '475 patent.

In view of the above evidence and foregoing statements, Applicant respectfully requests that the Examiner reconsider and withdraw the §102 rejection of claims 1-3, 6-10, and 13-14.

### **Rejections Under 35 U.S.C. §103**

The Examiner maintained the rejection of claims 4-5 and 11-12 under 35 U.S.C. §103(a) as being unpatentable over Mechanic '475.

The arguments presented above in response to the rejection of claims as anticipated by Mechanic '475 and in previous responses are also applicable to the obviousness rejection. When considered as a whole for all of its teachings, Mechanic '475 does not teach or suggest suspending collagen fibrils in water to form a fabric. On the contrary, Mechanic '475 teaches away from suspending collagen fibrils in non-buffered solutions such as in water. Moreover, Mechanic '475 teaches only crosslinked collagen fibers. Accordingly, Mechanic '475 does not render obvious any claim which includes a limitation of suspending in water collagen fibrils that are not crosslinked.

In view of the foregoing, Applicant respectfully requests that the Examiner reconsider and withdraw the §103 rejection of claims 4-5 and 11-12.

CONCLUSION

In view of the foregoing remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time.

If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,  
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